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CLINICAL & BASIC RESEARCH

Stenotrophomonas maltophilia

An emerging opportunistic nosocomial pathogen in a tertiary care hospital in Al Batinah North Governorate, Oman

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الستينوتروفوموناس مالتوفيليا

أحد مسببات الأمراض الانتهازية الناشئة في مستشفيات الرعاية الثالثية في محافظة شمال الباطنة، عمان

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ABSTRACT: ***Objectives:*** *Stenotrophomonas maltophilia*, a Gram-negative non-fermentative bacillus, has emerged as an important nosocomial pathogen in recent years. It is intrinsically resistant to many antibiotics and has the ability to acquire antibiotic resistance by multiple mechanisms. Treating *Stenotrophomonas* infections, therefore, is a serious challenge for physicians. This study aimed to investigate the antibiotic susceptibility patterns and risk factors contributing to *S. maltophilia* infections. ***Methods:*** A retrospective cross-sectional study was conducted at Sohar Hospital in Sohar, Oman. The demographic, clinical and microbiological data of individuals from whom *S. maltophilia* was isolated between September 2016 and August 2019 were reviewed. Descriptive statistics were presented as frequencies and percentages. ***Results:*** A total of 41 *S. maltophilia* isolates from clinical specimens of 41 patients were studied. Infection occurred predominantly in males (73%) and the majority of patients (88%) were either ≤5 years old or >60 years old. All inpatients had at least one comorbidity while 50% had more than one. All inpatients were exposed to various medical interventions such as intensive care (44%), mechanical ventilation (41%), haemodialysis (25%), Foley's catheterisation (13%) and central venous lines (6%). Most patients (81%) were in hospital longer than two weeks. The susceptibility rates of *S. maltophilia* to minocycline (97%), trimethoprim-sulfamethoxazole (93%) and levofloxacin (92%) were high; the rate was lowest for ceftazidime (50%). ***Conclusion:*** *S. maltophilia* was found to be an important nosocomial opportunistic pathogen. Prolonged hospital stay and exposure to various medical interventions were key factors contributing to the development of infection. Minocycline and ceftazidime were found to be the most and least susceptible drugs, respectively.

Keywords: Nosocomial Infection; Opportunistic Infections; Fluoroquinolones; Hemodialysis; Ventilation; Oman.

الملخص: الهدف: الستينوتروفوموناس مالتوفيليا ، هي عصيات غير مخمرة سالبة الجرام، ظهرت كمرض ميكروبي مهم في المستشفيات في السنوات الأخيرة. وهذه البكتريا لديها مقاومة للعديد من المضادات الحيوية ولديها القدرة على اكتساب مقاومة للمضادات الحيوية بآليات متعددة. لذلك ، فإن علاج عدوى الستينوتروفوموناس مالتوفيليا يمثل تحديًا خطيرًا للأطباء. هدفت هذه الدراسة إلى التحقق من أنماط الحساسية للمضادات الحيوية وعوامل الخطر التي تسهم في عدوى الستينوتروفوموناس مالتوفيليا. **الطريقة:** أجريت دراسة مستعرضة استرجاعية في مستشفى صحار، عمان. تمت مراجعة البيانات الديموغرافية والسريرية والميكروبيولوجية للأفراد الذين تم عزل الستينوتروفوموناس مالتوفيليا فيهم خلال الفترة بين سبتمبر 2016 وأغسطس 2019. تم عمل الإحصاء الوصفي على شكل تكرارات ونسب مئوية. **النتائج:** تمت دراسة ما مجموعه 41 عزلة من الستينوتروفوموناس مالتوفيليا من العينات السريرية لـ 14 مريضا. حدثت العدوى في الغالب عند الذكور (73%) وكانت غالبية المرضى (88%) مابين عمر خمس سنوات و 60 سنة. كان لدى جميع المرضى المرقدين مرض مزمن واحد على الأقل بينما كان لدى 50% أكثر من واحد. تعرض جميع المرضى المرقدين لتدخلات طبية مختلفة مثل العناية المركزة (44%)، والتهوية الميكانيكية (41%)، والغسيل الكلوي (25%)، وقسطرة فولي (13%) والخطوط الوريدية المركزية (6%). بقي معظم المرضى (81%) في المستشفى لمدة تزيد عن أسبوعين. كانت معدلات حساسية الستينوتروفوموناس مالتوفيليا للمينوسيكلين (97%)، و التريميثوبريم-سلفاميثوكسازول (93%) والليفوفلوكساسين (92%) وهي نسب مرتفعة. كانت الحساسية لعقارلسيفتازيديم في المعدل الأدنى (50%). **الخلاصة:** الستينوروفوموناس مالتوفيليا هي أحد مسببات الأمراض الانتهازية في المستشفيات. كانت الإقامة المطولة في المستشفى والتعرض للتدخلات الطبية المختلفة من العوامل الرئيسية التي ساهمت في حدوث العدوى. وجد أن المينوسكلين أكثر الأدوية تأثيرعلى هذه البكتيرياوالسيفتازيديم هو الأقل على التوالي.

الكلمات المفتاحية: عدوى المستشفيات؛ العدوى الانتهازية؛ الفلوروكينولونات؛ غسيل الكلى؛ التنفس؛ عمان.

Advances in Knowledge

- *Stenotrophomonas maltophilia infection predominantly occurred in males and in the younger and older age groups.*
- *S. maltophilia have shown good susceptibility to all tested antibiotics.*
- *S. maltophilia was most sensitive to minocycline and least susceptible to Ceftazidime.*

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Application to Patient Care

- *Incidence, risk factors and pattern and rate of antimicrobial resistance among S. maltophilia strains vary widely between regions. Regularly determining the prevalence of S. maltophilia and antibiotic resistance patterns and updating physicians' knowledge regarding this opportunistic organism will result in better management of S. maltophilia infection.*
- *Patients would benefit in terms of controlling antimicrobial resistance, reducing treatment failure and lessening mortality rates and financial burden.*

Stenotrophomonas maltophilia, formerly known as *Xanthomonas maltophilia*, is an aerobic, non-fermentative Gram-negative bacillus (NFGNB), widely distributed in almost all humid environments including hospital settings.[1–3] It survives on almost any humid surface and has been isolated from hospital equipment and supplies including mechanical ventilators, heart-lung machines, indwelling devices (i.e. endotracheal tubes, central venous and urinary catheters), haemodialysis units, endoscopes, nebulisers, disinfectants, hand wash solutions and intravenous fluids.[4–7] Although generally considered an asymptomatic coloniser or organism of low virulence, *S. maltophilia* has evolved in the past two decades to become an important opportunistic nosocomial pathogen, especially in critically ill patients.[8–13]

Bypassing natural body defences is pivotal for the development of *Stenotrophomonas* infections.[1–7] The infections are particularly common among very young and very old immunocompromised individuals and in patients with chronic respiratory illness, cystic fibrosis, neutropaenia and other immunodeficiency disorders.[4,7–10] The risk factors for *S. maltophilia* infection include prolonged mechanical ventilation, use of indwelling devices, previous exposure to broad-spectrum antibiotics and parenteral nutrition therapy.[4,6–8] *S. maltophilia* is the third most common NFGNB associated with nosocomial infections next to *P. aeruginosa* and *Acinetobacter baumannii*.[11] It is associated with a wide range of infections with pneumonia and bloodstream infections being the two most common manifestations.[14] Meningitis, brain abscess, urinary tract infection, skin and soft tissue infection, endocarditis and ocular and ear infections are less frequently seen infections caused by *S. maltophilia*.[1,4,5,7]

S. maltophilia-associated infections pose serious treatment challenges because they are intrinsically resistant to many antibiotics including aminoglycosides and carbapenems and the bacillus has the ability to acquire resistance to antimicrobial agents by multiple mechanisms.[4,14,15] Numerous studies have reported trimethoprim-sulfamethoxazole (TMP-SMX) as the antibiotic of choice for treating *S. maltophilia* infections.[14–16] Fluoroquinolones, minocycline and ceftazidime were also found to be effective drugs.[4,16–18] However, recent studies have reported alarming increases in the resistance of *Stenotrophomonas* to these agents.[1,12] Furthermore, its ability to form biofilm and quorum sensing has posed treatment challenges especially in critically ill patients in intensive care units (ICUs).[1,9,15] There is a paucity in the literature of studies on *S. maltophilia* in Al Batinah North governorate, Oman. Hence, the present study aimed to investigate the antimicrobial susceptibility of *S. maltophilia* isolated at Sohar Hospital's Microbiology Laboratory, Sohar, and reveal related clinical backgrounds such as the spectrum of infection, comorbidity and underlying risk factors contributing to infection.

Methods

This retrospective cross-sectional study was conducted at a 400-bed referral ministry hospital in Al Batinah North governorate, Oman. The clinical and microbiological data of 41 *S. maltophilia* isolates that grew from clinical samples from September 2016 to August 2019 were retrieved from microbiology laboratory records and the Al-Shifa electronic medical records system. The collected information included patients' demographic characteristics, length of hospital stay, comorbidities at the time of admission, exposure to medical equipment and instruments, site of infection and the type of clinical specimen processed in the laboratory.

All the strains of *S. maltophilia* isolated from sterile sites such as blood and cerebral spinal fluid and the strains isolated from sites such as skin, mucus membranes, wounds and endotracheal tubes in the presence of clinical signs and symptoms were considered infections and included in the study. *S. maltophilia* isolated from non-sterile sites such as skin, mucus membranes, wounds and endotracheal tubes in the absence of clinical signs and symptoms were considered colonisation and excluded from the study. Repeat isolates from all clinical samples were excluded.

S. maltophilia isolates were recovered from different clinical samples including blood, urine and respiratory secretions. The isolates were identified by standard microbiological methods and the automated Vitek® 2 system (bioMérieux SA, Lyon, France).

Table 1: Demographic and clinical characteristics of patients infected with *Stenotrophomonas maltophilia* at a tertiary care hospital in Al Batinah North Governorate, Oman (N = 41)

Characteristic	n (%)
Age in years	
<1	7 (17)
1–5	7 (17)
6–30	0 (0)
31–60	5 (12)
>60	22 (54)
Gender	
Male	30 (73)
Female	11 (27)
Duration of hospital stay (n = 32)	
<2 days	2 (6)
3–7 days	4 (13)
2–4 weeks	11 (34)
>4 weeks	15 (47)
Source/site of organism isolation*	
Respiratory secretions	15 (37)
Blood	13 (32)
Urine	5 (12)
Wound/pus swab	3 (7)
Eye swab	2 (5)
Ear swab	1 (2)
Synovial fluid	1 (2)
Cerebrospinal fluid	1 (2)

**Six S. maltophilia strains were isolated from the clinical samples received from other hospitals, and three strains were isolated from the patients treated in the outpatient department*

Antimicrobial susceptibility testing was performed using Kirby-Bauer's disc diffusion method on Mueller-Hinton agar with the following antibiotic panel by using Oxoid™ antibiotic susceptibility disks (Thermo Fisher Scientific, Waltham, Massachusetts, USA): levofloxacin (5 µg), TMP-SMX (1.25/23.75 µg) and minocycline (30 µg). For ceftazidime, a minimum inhibitory concentration was determined by the Epsilometer test (Etest), as recommended by the Clinical Laboratory Standards Institute.[19] Quality control was performed using *Escherichia coli* (ATCC 25922) and *P. aeruginosa* (ATCC 27853).

The data obtained were entered and analysed using Statistical Package for Social Sciences (SPSS), Version 22 (IBM, Corp., Armonk, New York, USA). Descriptive statistics for all variables were derived using Epi Info 7 for Windows (Centers for Disease Control and Prevention, Atlanta, Georgia, USA) and stated mainly as frequency and percentages. Antibiotic susceptibility was interpreted as sensitive or resistant.

This study was approved by the Research and Ethical Committee of the Ministry of Health in Oman (MH/DHSG/NBG/1923195718/2019).

Table 2: Comorbidity and underlying risk factors of in-patients with *Stenotrophomonas maltophilia* infection at a tertiary care hospital in Al Batinah North Governorate, Oman (N = 32)

Comorbidity/Risk factor	n (%)
Presence of one comorbidity	32 (100)
Presence of more than one comorbidity	16 (50)
Type of cormobidity	
Cardiovascular diseases (hypertension, IHD, CHD, etc.)	16 (50)
Chronic renal diseases (end stage renal disease)	9 (28)
Pulmonary diseases	8 (25)
Diabetes	8 (25)
Congenital/inherited diseases*	7 (22)
CNS disorders	5 (16)
Liver cirrhosis and oesophageal varices	1 (3)
Underlying risk factor	
ICU admission	14 (44)
Mechanical ventilation	13 (41)
Haemodialysis	8 (25)
Foley's catheterisation	4 (13)
Central venous line	2 (6)
Length of hospital stay >two weeks	26 (81)

IHD = ischaemic heart disease; CHD = congenital heart disease; CNS = central nervous system; ICU = intensive care unit.

**One patient each had cystic fibrosis, Guillain-Barré syndrome, Hirschprung's disease, cerebral palsy, Dandy Walker's disease, Krebs' disease and congenital heart disease.*

Table 3: Antibiotic susceptibility pattern of *Stenotrophomonas maltophilia*

Antibiotic	Antibiotic susceptibility in %	
	Sensitive	Resistance
TMP-SMX	93	7
*Ceftazidime	50	50
Levofloxacin	92	8
Minocycline	97	3

TMP-SMX = trimethoprim-sulfamethoxazole.

**Antibiotic sensitivity tested by Epsilometer test.*

Results

A total of 41 *S. maltophilia* isolates from various clinical samples received at Sohar Hospital's Microbiology Laboratory were reviewed. *S. maltophilia* was predominantly isolated from males (73%) compared to females (27%). The majority of the patients (88%) were ≤five years old (34%) or >60 years old (54%). Most patients (78%) were inpatients and had a hospital stay of at least two weeks (81%) [Table 1].

All inpatients had one comorbidity while 50% had more than one comorbid conditions such as cardiovascular disease (50%), chronic renal disease (28%), pulmonary disease (25%), diabetes (25%), congenital/inherited diseases (22%) or central nervous system disorders (16%). All inpatients had undergone medical interventions including being admitted to the intensive care unit (44%), mechanical ventilation (41%), haemodialysis (25%), Foley's catheterisation (13%) or the insertion of central venous lines (6%). With respect to the source, *S. maltophilia* was isolated most frequently from blood (32%) followed by endotracheal secretions (24%), sputum (12%), urine (12%), swabs of wounds (7%), eyes (5%) and ears (2%) and synovial (2%) and cerebrospinal (2%) fluid [Table 2].

In the present study, the *in vitro* susceptibility rate of *S. maltophilia* was highest for minocycline (97%) followed by TMP-SMX (93%) and levofloxacin (92%). However, only 50% of *S. maltophilia* samples showed resistance to ceftazidime [Table 3].

Discussion

S. maltophilia, previously considered a coloniser, has emerged as an important nosocomial pathogen within the past few decades, especially in severely immunodeficient individuals. It can cause serious infections and treating these associated infections can pose a serious challenge because of limited therapeutic options and the rapid development of antimicrobial resistance. The present study investigated antibiotic susceptibility patterns as well as underlying risk factors in patients who acquired *S. maltophilia* infections.

The present study observed a predominance of *S. maltophilia* isolation from males. Most patients had either an immature or weakened immune system and were ≤5 or >60 years of age (88%); these findings were consistent with previous studies.[7,8] Additionally, all patients had one (100%) while some (50%) had more than one comorbidity such as pulmonary or chronic kidney disease, diabetes or congenital/inherited disorders. In a similar study, Kim *et al*. demonstrated the association of *S. maltophilia* infection with a variety of comorbid conditions.[20] An important feature of *S. maltophilia* is its ability to asymptomatically colonise biotic or abiotic surfaces due to the formation of biofilm rather than infection, which is often associated with an individual's decreased immune status.[18,20] Invasive procedures (e.g. mechanical ventilation, central venous line, Foley's catheterisation and haemodialysis), receiving medical attention in intensive care facilities, prolonged length of hospital stay (more than two weeks), exposure to broad-spectrum antibiotics and immunocompromised status were found to be key underlying risk factors for *S. maltophilia* infections.[18,20] Risk factors in the present study group were similar to previous reports.[1,12,21]

S. maltophilia has developed extensive resistance to most commonly used antibiotics including beta-lactams, cephalosporins and macrolides and is intrinsically resistant to carbapenems and aminoglycosides.[22] Susceptibility data are available for a limited number of antimicrobial agents such as TMP-SMX, fluoroquinolones such as levofloxacin and moxifloxacin, ceftazidime, minocycline and doxycycline.[14–15]

In the present study, most isolates (93%) were found to be susceptible to TMP-SMX. This finding is in line with but slightly lower than reports from Ismail *et al*. where all strains tested with an Etest showed susceptibility to TMP-SMX.[14] However, resistance rates, are increasing and 7% of strains showed resistance to TMP-SMX in the present study. This low-level resistance (2–10%) is in accordance with many previous studies.[9,14,23] A few outliers, however, have demonstrated high levels of resistance ranging from 10–25%.[7,24–26] TMP-SMX, therefore, can still be recommended as the first-line drug for empirical therapy of *S. maltophilia* infections.

Fluoroquinolones have become reasonable alternatives to treat *Stenotrophomonas* infections. Reports have shown that monotherapy with fluoroquinolones achieves equal efficacy to TMP-SMX.[26,27] The findings of the present study were consistent with many other studies that demonstrated potent *in vitro* susceptibility of fluoroquinolones against *S. maltophilia*.[26,27] In the present study, 92% of the strains demonstrated susceptibility to levofloxacin. This finding was slightly lower than was found in a study by Wu *et al*. in which all strains isolated from ocular infections were susceptible to levofloxacin and moxifloxacin.[26] However, several studies have revealed a resistance rate ranging from 10–50% to fluoroquinolones.[14,24,28,29] Hence, it is imperative to select antibiotics to treat *S. maltophilia* infection based on local antimicrobial sensitivity patterns. The clinical value of levofloxacin is greater as it has the advantage of biofilm disruption and achieving much higher concentrations than the minimum inhibitory concentration, especially in respiratory secretions.[5,14,24] These advantages make

levofloxacin a better choice among quinolones, especially to treat respiratory infections.

In the present study, most of the *S. maltophilia* isolates (97%) showed *in vitro* susceptibility to minocycline. This finding is in concordance with the results of Looney *et al*.[11] However, the clinical use of minocycline is still limited due to its ototoxicity, although it is highly effective against *Stenotrophomonas*.[11]

Among beta-lactams, anti-pseudomonal beta-lactams such as ceftazidime were previously considered to be the most effective drugs against *S. maltophilia*.[30] However, recent studies have demonstrated a high rate of resistance (>40%) to these antibiotics.[24,31,32] The present study results were congruent with the results of those studies, where half of the *Stenotrophomonas* strains showed resistance to these drugs, suggesting increased global resistant trends to cephalosporins.[24,31,32]

Owing to the rapid emergence of drug-resistant strains of *Stenotrophomonas* for monotherapy (with TMP-SMX, fluoroquinolones and other drugs), combination therapy with two or three antibiotics, especially in critical patients with serious infections, have been proposed by several researchers as a way to attain synergism and overcome drug resistance.[14,15] Gregory *et al*. demonstrated better *in vitro* bactericidal effects when using a combination of TMP-SMZ and moxifloxacin on *S. maltophilia* when compared to monotherapy.[15] Although there are not enough data on the *in vivo* efficacy of combination therapy, several studies have suggested the use of a combination of drugs for treating severe invasive infections, especially in immune-deficient individuals.[12,14,15]

The present study was subject to certain limitations. First, the sample size was small. Second, the study did not assess the prior antibiotic exposure and treatment outcomes of infected patients. Third, this study was retrospective; therefore, the culture results were not clinically correlated to determine whether they represented infection or colonisation accurately. Finally, this was a single-centre study in Oman; hence, the findings may not be generalisable.

Conclusion

S. maltophilia is an important emerging nosocomial opportunistic pathogen. Prolonged length of hospital stay and exposure to various invasive medical interventions were key factors contributing to infection. TMP-SMZ, levofloxacin and minocycline showed good *in vitro* susceptibility against *S. maltophilia* and are promising therapeutic options.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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References

1. Adegoke AA, Stenström TA, Okoh AI. Stenotrophomonas maltophilia as an emerging ubiquitous pathogen: Looking beyond contemporary antibiotic therapy. Front Microbiol 2017; 8:2276. https://doi.org/10.3389/fmicb.2017.02276.
2. Satish M, Mumtaz MA, Bittner MJ, Valenta C. Stenotrophomonas maltophilia endocarditis of an implantable cardioverter defibrillator lead. Cureus 2019; 11:e4165. https://doi.org/10.7759/cureus.4165.
3. Geller M, Nunes CP, Oliveira L, Nigri R. S. maltophilia pneumonia: A case report. Respir Med Case Rep 2018; 24:44–5. https://doi.org/10.1016/j.rmcr.2018.04.004.
4. Xun M, Zhang Y, Li BL, Wu M, Zong Y, Yin YM. Clinical characteristics and risk factors of infections caused by Stenotrophomonas maltophilia in a hospital in northwest China. J Infect Dev Ctries 2014: 8:1000–5. https://doi.org/10.3855/jidc.4236.
5. Wu H, Wang JT, Shiau YR, Wang HY, Lauderdale TL, Chang SC, et al. A multicenter surveillance of antimicrobial resistance on Stenotrophomonas maltophilia in Taiwan. J Microbiol Immunol Infect 2012; 45:120–6. https://doi.org/10.1016/j.jmii.2011.09.028.
6. Brooke JS. New strategies against Stenotrophomonas maltophilia: A serious worldwide intrinsically drug-resistant opportunistic pathogen. Expert Rev Anti Infect Ther 2014; 12:1–4. https://doi.org/10.1586/14787210.2014.864553.
7. Gajdács M, Urbán E. Prevalence and antibiotic resistance of Stenotrophomonas maltophilia in respiratory tract samples: A 10-year epidemiological snapshot. Health Serv Res Manag Epidemiol 2019; 6:2333392819870774. https://doi.org/10.1177/2333392819870774.
8. Singhal L, Kaur P, Gautam V. Stenotrophomonas maltophilia: From trivial to grievous. Indian J Med Microbiol 2017; 35:469–79. https://doi.org/10.4103/ijmm.IJMM_16_430.
9. Brooke JS. Stenotrophomonas maltophilia: An emerging global opportunistic pathogen. Clin Microbiol Rev 2012; 25:2–41. https://doi.org/10.1128/CMR.00019-11.
10. Murugesan S, Rudrapathy P, Samuel S. Emergence of unusual gram-negative bacteria among cancer patients in a tertiary care cancer centre at North Kerala. Online J Health Allied Sci 2018; 17:7.
11. Chawla K, Vishwanath S, Munim FC. Nonfermenting Gram-negative Bacilli other than Pseudomonas aeruginosa and Acinetobacter Spp. Causing Respiratory Tract Infections in a Tertiary Care Center. J Global Infect Dis 2013; 5:144–8.
12. Juhász E, Krizsán G, Lengyel G, Grósz G, Pongrácz J, Kristóf K. Infection and colonization by Stenotrophomonas maltophilia: Antimicrobial susceptibility and clinical background of strains isolated at a tertiary care centre in Hungary. Ann Clin Microbiol Antimicrob 2014; 13:333. https://doi.org/10.1186/s12941-014-0058-9.

13. Baidya A, Kodan P, Fazal F, Tsering S, Menon PR, Jorwal P, et al. Stenotrophomonas maltophilia: More than just a colonizer! Indian J Crit Care Med 2019; 23:434–6. https://doi.org/10.5005/jp-journals-10071-23241.

14. Ismail N, Zam Z, Hassan SA, Rahman ZA. A combination of trimethoprim-sulfamethoxazole and ceftazidime showed good in vitro activity against Stenotrophomonas maltophilia. Malays J Med Sci 2017; 24:21–7. https://doi.org/10.21315/mjms2017.24.2.3.

15. Gregory ER, Osborne SB, Gardner BM, Broughton RA. Trimethoprim/sulfamethoxazole and moxifloxacin therapy for a pediatric Stenotrophomonas maltophilia ventriculoperitoneal shunt infection. J Pediatr Pharmacol Ther 2019; 24:61–5. https://doi.org/10.5863/1551-6776-24.1.61.

16. Chang YT, Lin CY, Chen YH, Hsueh PR. Update on infections caused by Stenotrophomonas maltophilia with particular attention to resistance mechanisms and therapeutic options. Front Microbiol 2015; 6:893. https://doi.org/10.3389/fmicb.2015.00893.

17. Falagas ME, Valkimadi PE, Huang YT, Matthaiou DK, Hsueh PR. Therapeutic options for Stenotrophomonas maltophilia infections beyond co-trimoxazole: A systematic review. J Antimicrob Chemother 2008; 62:889–94. https://doi.org/10.1093/jac/dkn301.

18. Millán-Díaz B, González-Tabarés L, Cobelo-Casas C, López-Vázquez M, Calviño-Varela J. Stenotrophomonas maltophilia: A rare cause of peritonitis in CAPD patients. Nefrologia 2017; 37:646–7. https://doi.org/10.1016/j.nefro.2017.03.018.

19. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing. CLSI supplement M100. 27th ed. Wayne, Pennsylvania, USA: Clinical and Laboratory Standards Institute; 2017.

20. Kim EJ, Kim YC, Ahn JY, Jeong SJ, Ku NS, Choi JY, et al. Risk factors for mortality in patients with Stenotrophomonas maltophilia bacteremia and clinical impact of quinolone–resistant strains. BMC Infect Dis 2019; 19:754. https://doi.org/10.1186/s12879-019-4394-4.

21. Hotta G, Matsumura Y, Kato K, Nakano S, Yunoki T, Yamamoto M, et al. Risk factors and outcomes of Stenotrophomonas maltophilia bacteraemia: A comparison with bacteraemia caused by Pseudomonas aeruginosa and Acinetobacter species. PLoS One 2014; 9:e112208. https://doi.org/10.1371/journal.pone.0112208.

22. Brooke JS. New strategies against Stenotrophomonas maltophilia: a serious worldwide intrinsically drug-resistant opportunistic pathogen, Expert Rev Anti Infect Ther 2014; 12:1–4. https://doi.org/10.1586/14787210.2014.864553.

23. Toleman MA, Bennet PM, Bennet BM, Jones RN, Walsh TR. Global emergence of trimethoprim/sulfamethoxozole resistance in Stenotrophomonas maltophilia mediated by acquisition of sul genes. Emerg Infect Dis 2007; 13:559–65. https://doi.org/10.3201/eid1304.061378.

24. Farrell DJ, Sader HS, Jones RN. Antimicrobial susceptibilities of a worldwide collection of Stenotrophomonas maltophilia isolates tested against tigecycline and agents commonly used for S. maltophilia infections. Antimicrob Agents Chemother 2010; 54:2735–7. https://doi.org/10.1128/AAC.01774-09.

25. Gupta P, Kale P, Khillan V. Resurgence of global opportunistic multidrug-resistant Stenotrophomonas maltophilia. Indian J Crit Care Med 2018; 22:503–8. https://doi.org/10.4103/ijccm.IJCCM_106_18.

26. Wu AL, Yeh LK, Ma DH, Chen PY, Lin HC, Sun CC, et al. Clinical characteristics of Stenotrophomonas maltophilia keratitis. Cornea 2016; 35:795–800. https://doi.org/10.1097/ICO.0000000000000855.

27. Wang YL, Scipione MR, Dubrovskaya Y, Papadopoulos J. Monotherapy with fluoroquinolone or trimethoprim-sulfamethoxazole for treatment of Stenotrophomonas maltophilia infections. Antimicrob Agents Chemother 2014; 58:176–182. https://doi.org/10.1128/AAC.01324-13.

28. Cho SY, Kang CI, Kim J, Ha YE, Chung DR, Lee NY, et al. Can levofloxacin be a useful alternative to trimethoprim-sulfamethoxazole for treating Stenotrophomonas maltophilia bacteremia? Antimicrob Agents Chemother 2014; 58:581–3. https://doi.org/10.1128/AAC.01682-13.

29. Samonis G, Karageorgopoulos DE, Maraki, S, Levis P, Dimopoulou D, Spernovasilis NA, et al. Stenotrophomonas maltophilia infections in a general hospital: Patient characteristics, antimicrobial susceptibility, and treatment outcome. PLoS One 2012; 7:e37375. https://doi.org/10.1371/journal.pone.0037375.

30. Zhanel GG, Adam HJ, Baxter MR, Fuller J, Nichol KA, Denisuik AJ, et al. Antimicrobial susceptibility of 22746 pathogens from Canadian hospitals: Results of the CANWARD 2007-11 study. J Antimicrob Chemother 2013; 68:i7–22. https://doi.org/10.1093/jac/dkt022.

31. Chang YT, Lin CY, Chen YH, Hsueh PR. Update on infections caused by Stenotrophomonas maltophilia with particular attention to resistance mechanisms and therapeutic options. Front Microbiol 2015; 6:893. https://doi.org/10.3389/fmicb.2015.00893.

32. Chung HS, Hong SG, Lee Y, Kim M, Yong D, Jeong SH, et al. Antimicrobial susceptibility of Stenotrophomonas maltophilia isolates from a Korean tertiary care hospital. Yonsei Med J 2012; 53:439–44. https://doi.org/10.3349/ymj.2012.53.2.439.